Extract from Report of the Meeting of the Edinburgh and Lothians Branch of the Ataxia Group

at Lasswade High School Centre on Saturday 9th September 2000

Dr Adam Zeman's Talk

Andrea Bothwell, Branch Convener, welcomed Dr Zeman to the meeting. He is a consultant neurologist at the Western General Hospital in Edinburgh who is doing some research at the moment and sees quite a lot of people with Ataxia.

He explained the **cerebellum** first of all. It is almost a 'separate brain' at the base of the skull beneath the cerebral hemispheres. It's not known exactly what it does but it has a distinctive repetitive structure when seen under a microscope and is thought to enable a smoothing of movements carried out by the body.

Common symptoms are a slurring of speech (dysarthria), unsteady gait (gait ataxia) and clumsiness in the arms and legs (limb ataxia). Speech can be affected too because exact positioning of the tongue is not possible and balance is also poor because the constant adjustments needed cannot be made. Another symptom is called nystagmus, which is a wobbly movement of the eyes when looking out to the side.

Arm and leg problems may be 1. 'intention tremor', wobbling as the hand or foot nears a target, 2. dysmetria which is failing to reach a goal accurately by under or over shooting and 3.

dysdiadochokinesis, making alternating movements with an irregular rhythm as when turning your hand palm up, palm down, palm up etc.

Walking may include ‘wide-based gait’ with legs wide apart (because of balance problems) and difficulty in hopping or walking along a white line. Less common and/or less obvious symptoms may be 1. ‘hypotonia’ which is a floppiness in passive movement eg when your hand is dangling, 2. ‘titubation’ a wobbly tremor in the head (no, no or yes, yes) and 3. ‘torticollis’ or wry neck.

All of these symptoms are what a neurologist will look for when making a diagnosis of Ataxia – you won’t necessarily show all of them. Dr Zeman then went on to talk about the causes of **acquired ataxias** – which have not been inherited. There can be many different reasons including vascular (strokes), infections eg an after effect of chicken pox or even CJD (human ‘mad cow’ disease). Other causes can be inflammations such as MS (multiple sclerosis), traumatic (having received an injury to the head), Toxins such as alcohol or heavy metals like lead or mercury, and degenerative diseases which result in the loss of cells in the cerebellum.

Sometimes a tumour can be the cause or even a secondary effect of a tumour eg breast cancer – when the breast cancer is treated the ataxia can also disappear. Some epilepsy drugs can cause the symptoms to appear, or there could be a psychiatric cause. Lastly, there may be a rare structural reason in the brain. Hydrocephalus (water on the brain) affects the flow of spinal fluid and Arnold Chiari identified a condition where the brain is too low and the bottom of the cerebellum gets squeezed – which can be treated by surgery.

Dr Zeman then went on to talk about **inherited ataxias**. These can be split between complex syndromes which are not really understood yet and 'Pure ataxias' which can be classified between early and late onset. One of the recent big developments in research has been the ability, in some ataxias, to look at the DNA and pinpoint the genetic cause. In the last 10 years, SCAs (spinal cerebellar ataxia) numbers 1 to 8 have been identified, the most recent being SCA 8 in 1999. Samples kept from earlier years can be rechecked for more information. However, the interest is mainly academic at the moment in identification, as no treatments have been targeted yet.

There are **three main areas of research in CA** at the moment:

1. All SCAs have a problem with the **genetic code in the DNA**. This is like a 'recipe book' for the body to make proteins from strings of chemicals called amino acids. The code contains too many 'triplet repeats'– basically an ingredient 'CAG' incorrectly repeated too many times (20 or 30 times instead of 10 times). The research is trying to understand this process and why it causes problems in the cerebellum.

2. The second area of research is into the **'channels' in the walls of nerve cells** which allow certain chemicals eg calcium to pass through the wall - into or out of the cell. These channels are made of proteins and the wrong sort can cause ataxia, also epilepsy, migraine and paralysis in some unrelated conditions.

3. The third area of research is controversial. It is concerned with the **function of the cerebellum in learning** new movements and suggests that there may also be subtle problems with thinking, making it more difficult to switch the mind from one task to another.

Dr Zeman then went on to explain the difference between **Recessive** and **Dominant** inheritance. Everyone has 2 sets of chromosomes and a child inherits one from each parent. With **dominant** inheritance, the condition will develop if one chromosome is affected. The children of affected parents will have a 50:50 chance of inheriting the disorder, and if they do will pass it on to half of their children. There is usually a clear family history with dominant conditions.

In a **recessive** disorder such as **Friedreich's Ataxia**, will only develop if both chromosomes are affected. Both parents of an affected person will have been carriers of the disorder but are not likely to have the condition. Their children may inherit 2 faulty genes (in which case they will develop the disorder), or inherit only one gene (they will be a carrier) or will not inherit a faulty one at all.

Dr Zeman's own research is into **SCA 8.** There are many current results from the US and other researchers throughout the world and there is also a good genetics department at the Western general. Different researchers do collaborate (up to a point) but don't usually share results before their first publication.

There were then various questions and comments. Chris mentioned that the Ataxia Head Office is funding research into a possible link

between ataxia and **gluten (wheat) sensitivity.** The meaning of the term **'idiopathic ataxia'** was discussed; it means that the cause is unknown (not thought to be inherited, but can never be sure – if it is inherited, it is likely to be recessive). Dr Zeman commented that research into patient information is hampered by the Western General (in common with most hospitals) **destroying notes** after 8 years, which is not a long time in terms of the development of ataxia. They often have to retrieve information from patients' GPs, who keep records for much longer.

Andrea Bothwell, the Branch Convener, then thanked Dr Zeman for his interesting and informative talk.